FINAL STATEMENT OF REASONS AND PUBLIC REPORT
DEPARTMENT OF PESTICIDE REGULATION

Title 3. California Code of Regulations
Amend Sections 6000 and 6710
Pertaining to Pesticide Safety Studies Involving Human Participants

UPDATE OF THE INITIAL STATEMENT OF REASONS

The originally proposed regulatory action was noticed in the *California Regulatory Notice Register* on December 6, 2002.

During the 45-day public comment period, the Department of Pesticide Regulation (DPR) received comments on the originally proposed text from one individual. The comment is discussed under the heading, "Summary And Response To Comments Received" of this Final Statement of Reasons. After reviewing this comment, DPR agreed that the suggested revision should be included in a modified text. DPR prepared a "Notice of Modifications to Text of Proposed Changes in the Regulations Pertaining to Pesticide Safety Studies Involving Human Participants" and made it available to the commentor for a 15-day period. These documents were also posted on DPR's Web site. One letter of comment was received pertaining to the modified text.

DPR amended sections 6000 and 6710 of Title 3, California Code of Regulations (3 CCR). The pesticide regulatory program activities that will be affected by this action are those pertaining to pesticide worker safety.

DPR amended these sections to revise the process by which DPR approves scientific protocols for California-based pesticide exposure studies that involve human participants.

Before a pesticide can be offered for sale for use in California, it has to be registered by DPR. Applicants for pesticide product registrations must submit various studies to DPR that are applicable to the product. In addition, DPR scientists conduct field studies each year to monitor worker exposure to pesticides. These studies help develop better methods to evaluate exposure and to prevent overexposure. Pesticide exposure studies are necessary in order to provide reliable and accurate exposure estimates for risk assessment. Using human participants enables researchers to obtain more relevant data regarding human health effects than could be obtained from animal studies. Because of the wide variety of climatic conditions and the diversity of crops grown in California, researchers can conduct a wide variety of human exposure studies within the state.

Scientific studies are usually conducted according to a generally accepted or standardized procedure known as a protocol. A good protocol can help ensure that valid, consistent results are obtained. Carefully designed protocols are especially important when people will be exposed to pesticides during the study.

Section 6710 states that no person shall conduct any pesticide exposure study in California, which involves human participants, unless the DPR Director has given written approval of the protocol. The study shall be conducted in accordance with the approved protocol. Concurrent review of protocols by the Office of Environmental Health Hazard Assessment (OEHHA) is also required. Protocols are reviewed from an ethical perspective, and technical guidance on the conduct of the study may be provided as well.

Section 6710 covers what is to be included in a protocol for this type of study. Items to be addressed include, among others, pesticide labeling directions and rates to be used, proposed starting and completion dates of the study, background and justification for the study, study design, methods to be used, selection process for human participants, criteria for exclusion or inclusion of these participants, written consent, medical supervision, and compensation.

Former section 6710(c) required DPR to submit these protocols to an appropriate committee of a public or private California research university, which had an agreement with DPR to review protocols with regard to use of human participants in research. After an ethical review of the protocol, the committee made a recommendation to DPR regarding approval of the protocol. The DPR Director then made the final decision and informed the registrant of the decision.

DPR contracted with the University of California at San Francisco (UCSF) to have its Committee on Human Research (CHR) review protocols for studies to be conducted by DPR's Worker Health and Safety Branch scientists. For a fee, CHR also reviewed protocols for studies submitted to DPR by pesticide registrants, task forces, consultants, and others. DPR reviewed the protocols from a health and safety perspective and forwarded them to CHR for an ethical review.

On May 25, 2001, DPR noticed a proposed regulatory action in the *California Regulatory Notice Register* to amend section 6710(d) to reflect a fee increase charged by UCSF for the protocol reviews. On September 7, 2001, DPR adopted the proposed action and delivered the rulemaking file to the Office of Administrative Law (OAL) for approval. Soon after this, UCSF informed DPR that it would no longer be reviewing the protocols. DPR subsequently withdrew the rulemaking file from OAL on September 17, 2001.

Since that time, DPR attempted without success to find another public or private California university to review the protocols. Since the text of section 6710 was based upon the guidelines and requirements of CHR, it was necessary for DPR to completely revise it to provide an alternative means of ensuring appropriate ethical review of the protocols.

Human pesticide exposure studies provide reliable and accurate exposure estimates for risk assessment. Without the data provided by such studies, it would be difficult to make sound regulatory decisions regarding the safety and welfare of persons handling pesticides or working in areas where pesticides have been applied. However, the conduct of these studies does not

come without potential risk to the human participants involved. Section 6710 was specifically designed to ensure that the safety, general welfare, and human rights of the human participants in pesticide exposure studies (conducted in California) are not compromised. This has been accomplished by requiring that all human pesticide exposure studies adhere to a strict protocol that has been approved by an independent ethical review committee. The former regulation stipulated that "an appropriate committee of a public or private California research university" must perform the protocol review. Until recently, DPR had an agreement to have these reviews conducted by CHR of UCSF, but as previously stated in this document, this agreement has been cancelled. DPR has been unable to develop a similar agreement with another ethical review committee under the constraints of the existing regulations. As a consequence of not having a committee willing to review human pesticide exposure study protocols, other than the allowed exemption, no such studies could be conducted in California until the emergency regulations were adopted.

This inability to acquire human pesticide exposure data can inhibit DPR's efforts to establish regulations for pesticide use in the state. DPR's reevaluation process is one particular tool used to acquire the necessary data for studying health effects of pesticides. Because of reported adverse health effects associated with their use, two pesticide chemicals already registered in California--chloropicrin and cyfluthrin--have entered the reevaluation process. Reports have implicated cyfluthrin as the causative agent in several cases of respiratory irritation among workers. Chloropicrin is known to cause severe eye and skin irritation. These pesticides are already being used in California and workers and handlers have the potential for being exposed. Pursuant to the reevaluation, DPR is requiring chloropicrin registrants to conduct and submit the results of certain worker exposure studies and air quality monitoring from field and greenhouse applications. The emergency regulations and the proposed permanent regulations would not only allow the conduct of these critical studies in California, but would also provide a means for reviewing the ethical aspects of the study protocols.

A risk assessment has recently been completed for the pesticide DDVP. This is a commonly used organophosphate pesticide, overexposure to which is known to cause neurotoxic effects due to its cholinesterase inhibition. Based on this risk assessment, levels of exposure for persons associated with this pesticide may be excessive and the use of DDVP may require mitigation measures. By using data obtained from pesticide exposure studies involving human participants, appropriate regulatory decisions can be made that will minimize exposure and maximize the safety of persons, including homeowners, that are associated with this pesticide. However, other than the allowed exemptions, these studies cannot be conducted in California unless DPR continues to provide a means by which the protocols can be reviewed for ethical considerations. The intent of the emergency regulations adopted on July 18, 2002, and the proposed permanent regulations was to provide an effective mechanism to ensure that human exposure pesticide study protocols are reviewed from an ethical perspective and that such research will continue to be conducted. The acquisition of accurate human exposure data is valuable in order to develop

and implement appropriate mitigation strategies, thereby minimizing or eliminating a potential hazard to workers and handlers associated with pesticides.

The adopted regulations would require a study director to obtain an Institutional Review Board (IRB) to conduct the ethical review of a protocol involving a California pesticide study using human participants. The study director would be required to submit all protocols directly to the IRB. DPR would accept an IRB's review provided it meets the requirements as specified in Title 40, Code of Federal Regulations (CFR), Protection of Environment, Part 26 (Protection of Human Subjects). In overseeing the entire protocol review process, DPR will also consider recommendations from IRB and OEHHA prior to approving the protocol.

An IRB is an objective committee whose purpose is to review protocols of human pesticide exposure studies to ensure the safety and general welfare of the human participants, and to guarantee that their human rights are not violated. IRBs shall meet the requirements as specified in Title 40 CFR, Protection of Environment, Part 26 (Protection of Human Subjects), when conducting an ethical review of a protocol. The CFR specifies that each IRB must have at least five members with varying backgrounds (both scientific and nonscientific) and should be represented by both men and women. Each IRB shall include at least one member who is not affiliated with the institution, and no member may participate in the IRB's review in which the member has a conflicting interest. Persons appointing committee members vary between IRBs.

DPR adopted new definitions in section 6000. These definitions are needed to clarify for section 6710 what is meant by "human participant," "Institutional Review Board," and "study director." The definition of "pesticide exposure study" has been amended.

CHANGES TO THE TEXT OF PROPOSED REGULATIONS

DPR made sufficiently related changes to the text since it was originally proposed. These changes were in response to a comment received during the 45-day comment period.

DPR changed the process by which a protocol would be reviewed. A study director would now submit a protocol to DPR for review and provisionary determination of acceptability before the protocol is submitted to the IRB. In addition, the modified text provides clarity to protocol amendment requirements by specifying the information required to be submitted when making such request.

In the final text of the regulation, an additional nonsubstanitive change was made to section 6710(i) to clarify that all documentation pertaining to the renewal be submitted by the study director to DPR .

SUMMARY AND RESPONSE TO COMMENTS RECEIVED

Comments Received During the 45-Day Public Comment Period

DPR received one letter of comment regarding the originally proposed text. It was submitted by Sara Beth Watson, of Steptoe and Johnson, Attorneys at Law, on behalf of Stephen N. Wilhelm of the Chloropicrin Manufacturers Task Force.

Comment: DPR and OEHHA should review the protocol before its submission to the IRB.

Response: DPR agrees with this comment. DPR prepared a modified text of proposed regulations that incorporated this suggestion and noticed it for a 15-day comment period.

Comments Received During the 15-Day Public Comment Period

DPR received one letter of comment regarding the modified text of proposed regulations. It was also submitted by Sara Beth Watson, of Steptoe and Johnson, Attorneys at Law, on behalf of Stephen N. Wilhelm of the Chloropicrin Manufacturers Task Force (CMTF).

Comment: CMFT recommends that the proposed provision be modified to require IRB approval of the renewal only if the IRB approval will expire within three months from the Department's expiration date. If the IRB approval will remain valid for more than three months after the DPR expiration, the IRB should not have to issue an extra approval for renewal. Alternatively, DPR could require that DPR's approval period always be concurrent with the IRB approval period.

Response: As the regulation is currently written, the expiration date of any protocol approval is ultimately established by DPR's Director but shall never exceed the expiration date established by the IRB. This language is consistent with the current regulation and allows DPR to establish an expiration date based on the potential risks of a study. In addition, DPR is interested in receiving adequate documentation from the study director and IRB regarding research reviews specified in Title 40 CFR, Protection of Environment, Part 26 (Protection of Human Subjects). Title 40 CFR, Protection of Environment, Part 26 (Protection of Human Subjects) requires an IRB to conduct continuing review of research at intervals appropriate for the level of risk, but not less than one year. DPR believes that an IRB protocol approval is conditioned on the requirement to conduct at minimum an annual review of the research. Since DPR's protocol approval is granted in part on the documentation from an IRB, DPR believes it is important to receive information on research reviews before approving a protocol renewal. The renewal process described in section 6710(j) is not in conflict with Title 40 CFR, Protection of Environment, Part 26 (Protection of Human Subjects) nor will it require an IRB to institute a new procedure to meet DPR's regulations. While the language in the current proposed regulation does leave the option open for DPR to shorten the expiration period, DPR has not deemed it necessary to do so for any of its approvals. If such a situation should arise, DPR does not feel

that this would create a problem for the IRB. In the event that DPR did feel that it was necessary to establish an expiration date that was significantly sooner than the IRB's, a renewal request would simply be submitted to DPR and since IRB approval had been previously granted and would still be valid, an additional IRB review would not be necessary until expiration of IRB approval. Again, DPR would establish a new expiration date that would not continue beyond that of the IRB.

PUBLIC HEARING

DPR received no requests to hold a public hearing and no hearing was scheduled or held.

CONSULTATION WITH OTHER AGENCIES

DPR has consulted with the California Department of Food and Agriculture during the development of the text of proposed regulations as specified in FAC section 11454.2, and the February 6, 1992, Memorandum of Agreement which was developed as provided in section 11454.2.

As required by FAC section 12981, DPR has consulted with OEHHA during the development of the text of proposed regulations, and OEHHA played a part in the development of the regulations. DPR has also consulted with the Department of Industrial Relations and the University of California.

DPR also notified these agencies concerning the modified text of proposed regulations and took into consideration the comments received from OEHHA.

Copies of correspondence with these agencies are contained in the rulemaking file.

MANDATE ON LOCAL AGENCIES OR SCHOOL DISTRICTS

DPR has determined that the proposed regulatory action does not impose a mandate on local agencies or school districts requiring reimbursement by the State pursuant to Part 7 (commencing with section 17500) of Division 4 of the Government Code because the regulatory action does not constitute a "new program or higher level of service of an existing program" within the meaning of section 6 of Article XIII B of the California Constitution. DPR has also determined that no nondiscretionary costs or savings to local agencies or school districts will result from the proposed regulatory action.

ALTERNATIVES DETERMINATION

The Director has determined that no alternative considered by DPR would be more effective in carrying out the purpose for which this regulation is proposed, or would be as effective and less burdensome to affected private persons or businesses than the proposed regulatory change.

POSTING REQUIREMENT

Title 3 CCR, section 6110, states in part that, "The public report shall be posted on the official bulletin boards of the Department, and of each commissioner's office, and in each District office of the DPR [Division of Pest Management, Environmental Protection and Worker Safety] for 45 days." DPR has posted its Initial Statement of Reasons and Public Report on its official bulletin board, which consists of the Department's Internet Home Page <http://www.cdpr.ca.gov>. In addition, copies were provided to the offices listed above for posting.